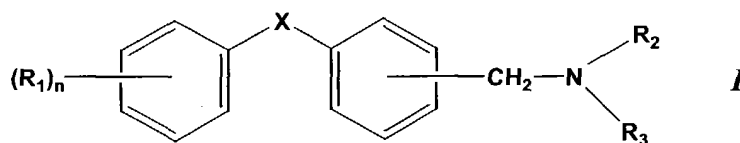


WHAT IS CLAIMED IS:

1. A compound of Formula I:



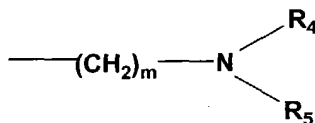
or a pharmaceutically-acceptable salt or solvate thereof, wherein:

$R_1$  is at each occurrence selected from the group consisting of halogen, optionally-substituted  $C_{1-6}$  alkyl, amino, nitro and cyano;

$n$  is an integer from 1 to 3;

$X$  is -O-, -S-, -NH-, -NHCH<sub>2</sub>-, -CH<sub>2</sub>NH-, -CH<sub>2</sub>-, -CH<sub>2</sub>O-, -OCH<sub>2</sub>-, -CH<sub>2</sub>S- or -SCH<sub>2</sub>-;

$R_2$  is

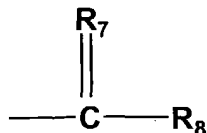


wherein:

$m$  is an integer from 2 to 4;

$R_4$  and  $R_5$  are independently selected from the group consisting of hydrogen and optionally-substituted  $C_{1-6}$  alkyl; or  $R_4$  and  $R_5$  together with the nitrogen to which they are attached form a ring having 4 or 5 carbon atoms, which ring optionally contains 1 or 2 additional heteroatoms independently selected from -O-, -S-, and -NR<sub>6</sub>-, wherein  $R_6$  is hydrogen,  $C_{1-6}$  alkyl,  $C_{1-6}$  haloalkyl or  $C_{1-6}$  hydroxyalkyl; and

$R_3$  is hydrogen, optionally-substituted  $C_{1-6}$  alkyl,

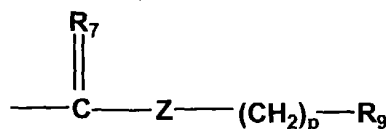


wherein:

R<sub>7</sub> is oxygen or sulfur; and

R<sub>8</sub> is selected from the group consisting of optionally-substituted C<sub>1-6</sub> alkyl, an optionally-substituted C<sub>3-8</sub> carbocyclic ring system and optionally-substituted C<sub>6-10</sub> aryl,

or R<sub>3</sub> is



wherein:

R<sub>7</sub> is oxygen or sulfur;

Z is -O- or -NH-;

*p* is an integer from 0 to 4; and

R<sub>9</sub> is selected from the group consisting of optionally-substituted C<sub>1-6</sub> alkyl, an optionally-substituted C<sub>3-8</sub> carbocyclic ring system, optionally-substituted C<sub>6-10</sub> aryl, optionally-substituted heteroaryl and optionally-substituted heterocycle, wherein the heterocycle is saturated or partially unsaturated;

*provided that,*

when R<sub>4</sub> and R<sub>5</sub> are independently hydrogen or C<sub>1-2</sub> alkyl, or when R<sub>4</sub> and R<sub>5</sub> together with the nitrogen to which they are attached form pyrrolidinyl, then X is not -S-;

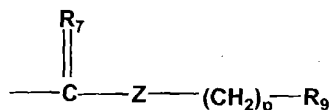
when X is -CH<sub>2</sub>O- and R<sub>3</sub> is hydrogen or methyl, then at least one of R<sub>4</sub> or R<sub>5</sub> is not C<sub>3-5</sub> alkyl; and

when X is -O- and R<sub>4</sub> and R<sub>5</sub> together with the nitrogen to which they are attached form a ring having 4 or 5 carbon atoms, then R<sub>8</sub> is not a C<sub>3</sub> carbocyclic ring system, and R<sub>9</sub> is not C<sub>3-5</sub> alkyl, phenyl, dihalophenyl or (C<sub>1-2</sub> alkyl)phenyl.

2. The compound according to claim 1, wherein  $n$  is 1.
3. The compound according to claim 1, wherein  $R_1$  is positioned *meta* relative to X.
4. The compound according to claim 1, wherein  $R_1$  is  $C_{1-6}$  haloalkyl.
5. The compound according to claim 1, wherein X include -O-.
6. The compound according to claim 1, wherein  $-CH_2-NR_2R_3$  is positioned *meta* relative to X.
7. The compound according to claim 1, wherein  $m$  is 2.
8. The compound according to claim 1, wherein  $R_4$  and  $R_5$  together with the nitrogen to which they are attached form a piperidyl ring.
9. The compound according to claim 1, wherein  $R_3$  is hydrogen or optionally-substituted  $C_{1-6}$  alkyl.
10. The compound according to claim 9, wherein  $R_3$  is hydrogen.
11. The compound according to claim 1, wherein  $R_3$  is  $\begin{array}{c} R_7 \\ || \\ -C- \\ | \\ R_8 \end{array}$ .
12. The compound according to claim 11, wherein  $R_7$  is oxygen.
13. The compound according to claim 11, wherein  $R_8$  is  $C_{1-6}$  alkyl,  $C_{5-6}$  cycloalkyl or optionally-substituted phenyl; wherein said optionally-substituted phenyl is optionally substituted once with halogen or  $C_{1-4}$  alkyl.

14. The compound according to claim 11, wherein  $R_8$  is acetyl, cyclopentanecarbonyl or *p*-fluorobenzoyl.

15. The compound according to claim 1, wherein  $R_3$  is



16. The compound according to claim 15, wherein  $R_7$  is oxygen.

17. The compound according to claim 15, wherein Z is -NH-.

18. The compound according to claim 15, wherein *p* is zero, 1, 2 or 3.

19. The compound according to claim 15, wherein  $R_9$  is  $C_{5-6}$  cycloalkyl, optionally-substituted phenyl and 5- to 6-membered saturated or partially unsaturated heterocycle, wherein said optionally-substituted phenyl is optionally substituted once with halogen or  $C_{1-4}$  alkyl.

20. The compound according to claim 15, wherein  $R_3$  is cyclohexylamino-carbonyl, 2-fluorophenylaminocarbonyl or 3-(morpholin-4-yl)-propylamino-thiocarbonyl.

21. The compound according to claim 1, wherein:

$R_3$  is hydrogen or optionally-substituted  $C_{1-6}$  alkyl;

$R_4$  and  $R_5$  together with the nitrogen to which they are attached form a ring having 4 or 5 carbon atoms, which ring optionally contains 1 or 2 additional heteroatoms independently selected from the group consisting of -O-, -S- and -NR<sub>6</sub>-, wherein  $R_6$  is hydrogen,  $C_{1-6}$  alkyl,  $C_{1-6}$  haloalkyl or  $C_{1-6}$  hydroxyalkyl; and

X is -O-, -CH<sub>2</sub>-O- or -CH<sub>2</sub>-S-.

22. The compound according to claim 1, wherein:

R<sub>3</sub> is hydrogen, C<sub>1-6</sub> alkyl, C<sub>1-6</sub> haloalkyl, C<sub>1-6</sub> hydroxyalkyl or C<sub>1-6</sub> alkyloxy(C<sub>1-6</sub>)alkyl;

R<sub>4</sub> and R<sub>5</sub> together with the nitrogen to which they are attached form a ring having 4 or 5 carbon atoms, which ring optionally contains 1 or 2 additional heteroatoms selected from the group consisting of -O-, -S-, and -NR<sub>6</sub>-, wherein R<sub>6</sub> is hydrogen or C<sub>1-6</sub> alkyl;

*n* is 1 or 2;

R<sub>1</sub> is halogen, C<sub>1-6</sub> alkyl or C<sub>1-6</sub> haloalkyl;

X is -O- or -CH<sub>2</sub>-O-; and

*m* is 2 or 3.

23. The compound according to claim 1, wherein:

R<sub>3</sub> is hydrogen or C<sub>1-6</sub> alkyl;

R<sub>4</sub> and R<sub>5</sub> together with the nitrogen to which they are attached form a ring having 4 or 5 carbon atoms, which ring optionally contains 1 additional heteroatom independently selected from the group consisting of -O-, -S- and -NR<sub>6</sub>-, wherein R<sub>6</sub> is hydrogen, C<sub>1-6</sub> alkyl, C<sub>1-6</sub> haloalkyl or C<sub>1-6</sub> hydroxyalkyl;

*n* is 1;

R<sub>1</sub> is C<sub>1-6</sub> haloalkyl;

X is -O-; and

*m* is 2.

24. The compound according to claim 1, wherein:

R<sub>3</sub> is hydrogen or optionally-substituted C<sub>1-6</sub> alkyl;

one of R<sub>4</sub> or R<sub>5</sub> is selected from the group consisting of hydrogen and optionally-substituted C<sub>1-6</sub> alkyl, and the other is selected from the group consisting of hydrogen, optionally-substituted C<sub>1-2</sub> alkyl and optionally-substituted C<sub>6</sub> alkyl; and

X is -O-, -CH<sub>2</sub>-O- or -CH<sub>2</sub>-S-.

25. The compound according to claim 1, wherein:

R<sub>3</sub> is hydrogen, C<sub>1-6</sub> alkyl, C<sub>1-6</sub> haloalkyl, C<sub>1-6</sub> hydroxyalkyl or C<sub>1-6</sub> alkyloxy(C<sub>1-6</sub>)alkyl;

one of R<sub>4</sub> or R<sub>5</sub> is selected from the group consisting of hydrogen, C<sub>1-6</sub> alkyl and C<sub>1-6</sub> haloalkyl, and the other is selected from the group consisting of hydrogen, C<sub>1-2</sub> alkyl, C<sub>6</sub> alkyl, C<sub>1-2</sub> haloalkyl and C<sub>6</sub> haloalkyl;

*n* is 1 or 2;

R<sub>1</sub> is halogen, C<sub>1-6</sub> alkyl or C<sub>1-6</sub> haloalkyl;

X is -O- or -CH<sub>2</sub>-O-; and

*m* is 2 or 3.

26. The compound according to claim 1, wherein:

R<sub>3</sub> is hydrogen or C<sub>1-6</sub> alkyl;

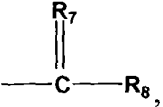
R<sub>4</sub> and R<sub>5</sub> are independently selected from the group consisting of hydrogen and C<sub>1-6</sub> alkyl;

*n* is 1;

R<sub>1</sub> is C<sub>1-6</sub> haloalkyl;

X is -O-; and

*m* is 2.

27. The compound according to claim 1, wherein R<sub>3</sub> is ,  
wherein:

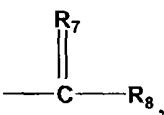
R<sub>7</sub> is oxygen or sulfur;

R<sub>8</sub> is optionally-substituted C<sub>1-6</sub> alkyl, optionally-substituted C<sub>5-8</sub> cycloalkyl or optionally-substituted C<sub>6-10</sub> aryl;

R<sub>4</sub> and R<sub>5</sub> together with the nitrogen to which they are attached form a ring having 4 or 5 carbon atoms, which ring optionally contains 1 or 2 additional heteroatoms independently selected from the group consisting of

-O-, -S- and -NR<sub>6</sub>-, wherein R<sub>6</sub> is hydrogen, C<sub>1-6</sub> alkyl, C<sub>1-6</sub> haloalkyl or C<sub>1-6</sub> hydroxyalkyl; and

X is -O-, -CH<sub>2</sub>-O- or -CH<sub>2</sub>-S-.

28. The compound according to claim 1, wherein R<sub>3</sub> is , wherein:

R<sub>7</sub> is oxygen;

R<sub>8</sub> is C<sub>1-6</sub> alkyl, C<sub>1-6</sub> haloalkyl, C<sub>1-6</sub> hydroxyalkyl, optionally-substituted C<sub>5-6</sub> cycloalkyl or optionally-substituted phenyl;

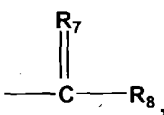
R<sub>4</sub> and R<sub>5</sub> together with the nitrogen to which they are attached form a ring having 4 or 5 carbon atoms, which ring optionally contains 1 or 2 additional heteroatoms selected from the group consisting of -O-, -S-, and -NR<sub>6</sub>-, wherein R<sub>6</sub> is hydrogen or C<sub>1-6</sub> alkyl;

n is 1 or 2;

R<sub>1</sub> is halogen, C<sub>1-6</sub> alkyl or C<sub>1-6</sub> haloalkyl;

X is -O- or -CH<sub>2</sub>-O-; and

m is 2 or 3.

29. The compound according to claim 1, wherein R<sub>3</sub> is , wherein:

R<sub>7</sub> is oxygen;

R<sub>8</sub> is C<sub>1-6</sub> alkyl, C<sub>5-6</sub> cycloalkyl or phenyl, wherein the phenyl is substituted with zero, 1 or 2 groups independently selected from the group consisting of halogen, C<sub>1-6</sub> alkyl, C<sub>1-6</sub> haloalkyl, C<sub>1-6</sub> hydroxyalkyl, C<sub>1-6</sub> alkyloxy(C<sub>1-6</sub>)alkyl, amino(C<sub>1-6</sub>)alkyl, hydroxy, nitro and amino;

R<sub>4</sub> and R<sub>5</sub> together with the nitrogen to which they are attached form a ring having 4 or 5 carbon atoms, which ring optionally contains 1 additional

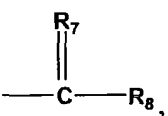
heteroatom independently selected from the group consisting of -O-, -S- and -NR<sub>6</sub>-, wherein R<sub>6</sub> is hydrogen, C<sub>1-6</sub> alkyl, C<sub>1-6</sub> haloalkyl or C<sub>1-6</sub> hydroxyalkyl;

*n* is 1;

R<sub>1</sub> is C<sub>1-6</sub> haloalkyl;

X is -O-; and

*m* is 2.

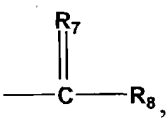
30. The compound according to claim 1, wherein R<sub>3</sub> is , wherein:

R<sub>7</sub> is oxygen or sulfur;

R<sub>8</sub> is optionally-substituted C<sub>1-6</sub> alkyl, optionally-substituted C<sub>3-8</sub> cycloalkyl or optionally-substituted C<sub>6-10</sub> aryl;

R<sub>4</sub> and R<sub>5</sub> are independently selected from the group consisting of hydrogen and optionally-substituted C<sub>1-6</sub> alkyl; and

X is -O-, -CH<sub>2</sub>-O- or -CH<sub>2</sub>-S-.

31. The compound according to claim 1, wherein R<sub>3</sub> is , wherein:

R<sub>7</sub> is oxygen;

R<sub>8</sub> is C<sub>1-6</sub> alkyl, C<sub>1-6</sub> haloalkyl, C<sub>1-6</sub> hydroxyalkyl, optionally-substituted C<sub>5-6</sub> cycloalkyl or optionally-substituted phenyl;

R<sub>4</sub> and R<sub>5</sub> are independently selected from hydrogen, C<sub>1-6</sub> alkyl and C<sub>1-6</sub> haloalkyl;

*n* is 1 or 2;

R<sub>1</sub> is halogen, C<sub>1-6</sub> alkyl or C<sub>1-6</sub> haloalkyl;

X is -O- or -CH<sub>2</sub>-O-; and

*m* is 2 or 3.



32. The compound according to claim 1, wherein  $R_3$  is  $\begin{array}{c} R_7 \\ || \\ -C-R_8 \end{array}$ ,  
wherein:

$R_7$  is oxygen;

$R_8$  is  $C_{1-6}$  alkyl,  $C_{5-6}$  cycloalkyl or phenyl, wherein the phenyl is substituted with zero, 1 or 2 groups independently selected from the group consisting of halogen,  $C_{1-6}$  alkyl,  $C_{1-6}$  haloalkyl,  $C_{1-6}$  hydroxyalkyl,  $C_{1-6}$  alkyloxy( $C_{1-6}$ )alkyl, amino( $C_{1-6}$ )alkyl, hydroxy, nitro and amino;

$R_4$  and  $R_5$  are independently selected from the group consisting of hydrogen and  $C_{1-6}$  alkyl;

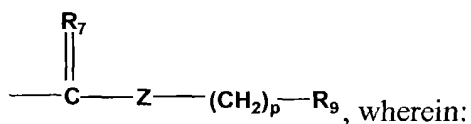
$n$  is 1;

$R_1$  is  $C_{1-6}$  haloalkyl;

$X$  is -O-; and

$m$  is 2.

33. The compound according to claim 1, wherein  $R_3$  is

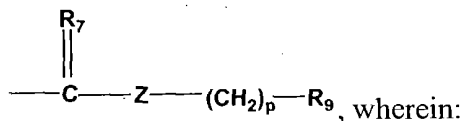


$R_9$  is optionally-substituted  $C_{1-2}$  alkyl, optionally-substituted  $C_6$  alkyl, optionally-substituted  $C_{3-8}$  cycloalkyl, substituted  $C_{6-10}$  aryl, optionally-substituted heteroaryl or optionally-substituted saturated or partially unsaturated heterocycle;

$R_4$  and  $R_5$  together with the nitrogen to which they are attached form a ring having 4 or 5 carbon atoms, which ring optionally contains 1 or 2 additional heteroatoms independently selected from the group consisting of -O-, -S- and -NR<sub>6</sub>-, wherein  $R_6$  is hydrogen,  $C_{1-6}$  alkyl,  $C_{1-6}$  haloalkyl or  $C_{1-6}$  hydroxyalkyl; and

$X$  is -O-, -CH<sub>2</sub>-O- or -CH<sub>2</sub>-S-.

34. The compound according to claim 1, wherein  $R_3$  is



$R_7$  is oxygen;

$Z$  is -NH-;

$p$  is zero, 1, 2 or 3;

$R_9$  is  $C_{1-2}$  alkyl,  $C_6$  alkyl,  $C_{1-6}$  haloalkyl,  $C_{1-6}$  hydroxyalkyl, optionally-substituted  $C_{5-6}$  cycloalkyl, substituted phenyl or optionally-substituted 5- to 6-membered saturated or partially unsaturated heterocycle;

$R_4$  and  $R_5$  together with the nitrogen to which they are attached form a ring having 4 or 5 carbon atoms, which ring optionally contains 1 or 2 additional heteroatoms selected from the group consisting of -O-, -S-, and -NR<sub>6</sub>-, wherein  $R_6$  is hydrogen or  $C_{1-6}$  alkyl;

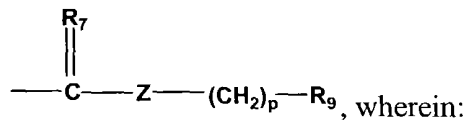
$n$  is 1 or 2;

$R_1$  is halogen,  $C_{1-6}$  alkyl or  $C_{1-6}$  haloalkyl;

$X$  is -O- or -CH<sub>2</sub>-O-; and

$m$  is 2 or 3.

35. The compound according to claim 1, wherein  $R_3$  is



$R_7$  is oxygen;

$Z$  is -NH-;

$p$  is zero, 1, 2 or 3;

$R_9$  is  $C_{5-6}$  cycloalkyl, substituted phenyl or 5- to 6-membered saturated or partially unsaturated heterocycle, where the substituted phenyl is phenyl substituted with 1 or 2 groups independently selected from the group consisting of halogen,  $C_{3-6}$  alkyl,  $C_{1-6}$  haloalkyl,  $C_{1-6}$  hydroxyalkyl,  $C_{1-6}$  alkyloxy( $C_{1-6}$ )alkyl, amino( $C_{1-6}$ )alkyl, hydroxy, nitro and amino, and where the substituted phenyl is not dihalophenyl;

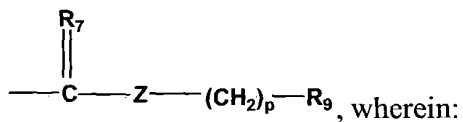
R<sub>4</sub> and R<sub>5</sub> together with the nitrogen to which they are attached form a ring having 4 or 5 carbon atoms, which ring optionally contains 1 additional heteroatom independently selected from -O-, -S- and -NR<sub>6</sub>-, wherein R<sub>6</sub> is hydrogen, C<sub>1-6</sub> alkyl, C<sub>1-6</sub> haloalkyl or C<sub>1-6</sub> hydroxyalkyl; *n* is 1;

R<sub>1</sub> is C<sub>1-6</sub> haloalkyl;

X is -O-; and

*m* is 2.

36. The compound according to claim 1, wherein R<sub>3</sub> is

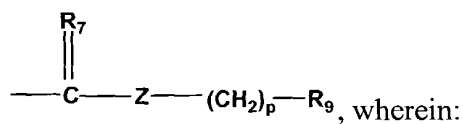


R<sub>9</sub> is optionally-substituted C<sub>1-6</sub> alkyl, optionally-substituted C<sub>3-8</sub> cycloalkyl, optionally-substituted C<sub>6-10</sub> aryl, optionally-substituted heteroaryl or optionally-substituted saturated or partially unsaturated heterocycle;

R<sub>4</sub> and R<sub>5</sub> are independently selected from the group consisting of hydrogen and optionally-substituted C<sub>1-6</sub> alkyl; and

X is -O-, -CH<sub>2</sub>-O- or -CH<sub>2</sub>-S-.

37. The compound according to claim 1, wherein R<sub>3</sub> is



R<sub>7</sub> is oxygen;

Z is -NH-;

*p* is zero, 1, 2 or 3;

R<sub>9</sub> is C<sub>1-6</sub> alkyl, C<sub>1-6</sub> haloalkyl, C<sub>1-6</sub> hydroxyalkyl, optionally-substituted C<sub>5-6</sub> cycloalkyl, optionally-substituted phenyl or optionally-substituted 5- to 6-membered saturated or partially unsaturated heterocycle;

R<sub>4</sub> and R<sub>5</sub> are independently selected from the group consisting of hydrogen, C<sub>1-6</sub> alkyl and C<sub>1-6</sub> haloalkyl;

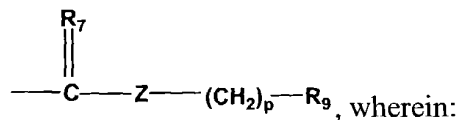
*n* is 1 or 2;

R<sub>1</sub> is halogen, C<sub>1-6</sub> alkyl or C<sub>1-6</sub> haloalkyl;

X is -O- or -CH<sub>2</sub>-O-; and

*m* is 2 or 3.

38. The compound according to claim 1, wherein R<sub>3</sub> is



R<sub>7</sub> is oxygen;

Z is -NH-;

*p* is zero, 1, 2 or 3;

R<sub>9</sub> is C<sub>5-6</sub> cycloalkyl, optionally-substituted phenyl or 5- to 6-membered saturated or partially unsaturated heterocycle, wherein the phenyl is substituted with zero, 1 or 2 groups independently selected from the group consisting of halogen, C<sub>1-6</sub> alkyl, C<sub>1-6</sub> haloalkyl, C<sub>1-6</sub> hydroxyalkyl, C<sub>1-6</sub> alkyloxy(C<sub>1-6</sub>)alkyl, amino(C<sub>1-6</sub>)alkyl, hydroxy, nitro and amino;

R<sub>4</sub> and R<sub>5</sub> are independently selected from the group consisting of hydrogen and C<sub>1-6</sub> alkyl;

*n* is 1;

R<sub>1</sub> is C<sub>1-6</sub> haloalkyl;

X is -O-; and

*m* is 2.

39. A compound selected from the group consisting of

*N*-(2-piperidin-1-ylethyl)-*N*-[3-(3-trifluoromethylphenoxy)benzyl]amine;

*N*-(2-piperidin-1-ylethyl)-*N*-[3-(3-trifluoromethylphenoxy)benzyl]-acetamide;

*N*-(2-piperidin-1-ylethyl)-*N*-[3-(3-trifluoromethylphenoxy)benzyl]-cyclopentane carboxamide;

*N*-(2-piperidin-1-ylethyl)-*N*-[3-(3-trifluoromethylphenoxy)benzyl]-4-fluorobenzamide;

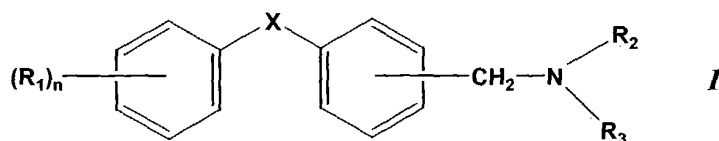
*N'*-cyclohexyl-*N*-(2-piperidin-1-ylethyl)-*N*-[3-(3-trifluoromethylphenoxy)-benzyl]urea;

*N'*-(2-fluorophenyl)-*N*-(2-piperidin-1-ylethyl)-*N*-[3-(3-trifluoromethylphenoxy)benzyl]urea; and

*N'*-[3-(morpholin-4-yl)propyl]-*N*-(2-piperidin-1-ylethyl)-*N*-[3-(3-trifluoromethylphenoxy)benzyl]thiourea;  
and pharmaceutically-acceptable salts thereof.

40. A pharmaceutical composition comprising the compound according to claim 1, or a pharmaceutically-acceptable salt thereof, and a pharmaceutically-acceptable carrier or diluent.

41. A method for treating, preventing or ameliorating a disorder responsive to blockage of sodium ion channels in a mammal suffering therefrom, comprising administering to said mammal in need of such treatment an effective amount of a compound of Formula *I*



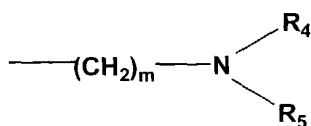
or a pharmaceutically-acceptable salt or solvate thereof, wherein:

$R_1$  is at each occurrence independently selected from the group consisting of hydrogen, halogen, optionally-substituted  $C_{1-6}$  alkyl, amino, nitro and cyano;

$n$  is an integer from 1 to 3;

$X$  is -O-, -S-, -NH-, -NHCH<sub>2</sub>-, -CH<sub>2</sub>NH-, -CH<sub>2</sub>-, -CH<sub>2</sub>O-, -OCH<sub>2</sub>-, -CH<sub>2</sub>S- or -SCH<sub>2</sub>-;

$R_2$  is

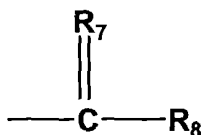


wherein:

$m$  is an integer from 2 to 4;

$\text{R}_4$  and  $\text{R}_5$  are independently selected from hydrogen and optionally-substituted  $\text{C}_{1-6}$  alkyl; or  $\text{R}_4$  and  $\text{R}_5$  together with the nitrogen to which they are attached form a ring having 4 or 5 carbon atoms, which ring optionally contains 1 or 2 additional heteroatoms independently selected from -O-, -S-, and -NR<sub>6</sub>-, wherein  $\text{R}_6$  is hydrogen,  $\text{C}_{1-6}$  alkyl,  $\text{C}_{1-6}$  haloalkyl or  $\text{C}_{1-6}$  hydroxyalkyl; and

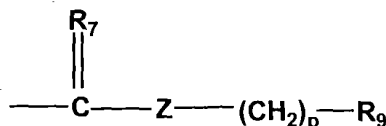
$\text{R}_3$  is hydrogen, optionally-substituted  $\text{C}_{1-6}$  alkyl,



wherein:

$\text{R}_7$  is oxygen or sulfur; and

$\text{R}_8$  is selected from optionally-substituted  $\text{C}_{1-6}$  alkyl, an optionally-substituted  $\text{C}_{3-8}$  carbocyclic ring system and optionally-substituted  $\text{C}_{6-10}$  aryl, or  $\text{R}_3$  is



wherein:

$\text{R}_7$  is oxygen or sulfur;

$\text{Z}$  is -O- or -NH-;

$p$  is an integer from zero to 4; and

$\text{R}_9$  is selected from optionally-substituted  $\text{C}_{1-6}$  alkyl, an optionally-substituted  $\text{C}_{3-8}$  carbocyclic ring system, optionally-substituted  $\text{C}_{6-10}$  aryl, optionally-

substituted heteroaryl and optionally-substituted heterocycle, wherein the heterocycle is saturated or partially unsaturated.

42. The method according to claim 41, wherein:

R<sub>3</sub> is hydrogen or optionally-substituted C<sub>1-6</sub> alkyl;

R<sub>4</sub> and R<sub>5</sub> together with the nitrogen to which they are attached form a ring having 4 or 5 carbon atoms, which ring optionally contains 1 or 2 additional heteroatoms independently selected from the group consisting of -O-, -S- and -NR<sub>6</sub>-, wherein R<sub>6</sub> is hydrogen, C<sub>1-6</sub> alkyl, C<sub>1-6</sub> haloalkyl or C<sub>1-6</sub> hydroxyalkyl; and

X is -O-, -S-, -CH<sub>2</sub>-O- or -CH<sub>2</sub>-S-.

43. The method according to claim 41, wherein:

R<sub>3</sub> is hydrogen, C<sub>1-6</sub> alkyl, C<sub>1-6</sub> haloalkyl, C<sub>1-6</sub> hydroxyalkyl or C<sub>1-6</sub> alkyloxy(C<sub>1-6</sub>)alkyl;

R<sub>4</sub> and R<sub>5</sub> together with the nitrogen to which they are attached form a ring having 4 or 5 carbon atoms, which ring optionally contains 1 or 2 additional heteroatoms selected from the group consisting of -O-, -S-, and -NR<sub>6</sub>-, wherein R<sub>6</sub> is hydrogen or C<sub>1-6</sub> alkyl;

*n* is 1 or 2;

R<sub>1</sub> is halogen, C<sub>1-6</sub> alkyl or C<sub>1-6</sub> haloalkyl;

X is -O- or -S-; and

*m* is 2 or 3.

44. The method according to claim 41, wherein:

R<sub>3</sub> is hydrogen or C<sub>1-6</sub> alkyl;

R<sub>4</sub> and R<sub>5</sub> together with the nitrogen to which they are attached form a ring having 4 or 5 carbon atoms, which ring optionally contains 1 additional heteroatom independently selected from the group consisting of -O-, -S- and -NR<sub>6</sub>-, wherein R<sub>6</sub> is hydrogen, C<sub>1-6</sub> alkyl, C<sub>1-6</sub> haloalkyl or C<sub>1-6</sub> hydroxyalkyl;

*n* is 1;

$R_1$  is  $C_{1-6}$  haloalkyl;

X is -O-; and

$m$  is 2.

45. The method according to claim 41, wherein:

$R_3$  is hydrogen or optionally-substituted  $C_{1-6}$  alkyl;

$R_4$  and  $R_5$  are independently selected from the group consisting of hydrogen and optionally-substituted  $C_{1-6}$  alkyl; and

X is -O-, -S-, -CH<sub>2</sub>-O- or -CH<sub>2</sub>-S-.

46. The method according to claim 41, wherein:

$R_3$  is hydrogen,  $C_{1-6}$  alkyl,  $C_{1-6}$  haloalkyl,  $C_{1-6}$  hydroxyalkyl or  $C_{1-6}$  alkyloxy( $C_{1-6}$ )alkyl;

$R_4$  and  $R_5$  are independently selected from the group consisting of hydrogen,  $C_{1-6}$  alkyl and  $C_{1-6}$  haloalkyl;

$n$  is 1 or 2;

$R_1$  is halogen,  $C_{1-6}$  alkyl or  $C_{1-6}$  haloalkyl;

X is -O- or -S-; and

$m$  is 2 or 3.

47. The method according to claim 41, wherein:

$R_3$  is hydrogen or  $C_{1-6}$  alkyl;

$R_4$  and  $R_5$  are independently selected from the group consisting of hydrogen and  $C_{1-6}$  alkyl;

$n$  is 1;

$R_1$  is  $C_{1-6}$  haloalkyl;

X is -O-; and

$m$  is 2.



48. The method according to claim 41, wherein  $R_3$  is  $\begin{array}{c} R_7 \\ || \\ -C-R_8 \end{array}$ ,  
wherein:

$R_7$  is oxygen or sulfur;

$R_8$  is optionally-substituted  $C_{1-6}$  alkyl, optionally-substituted  $C_{3-8}$  cycloalkyl or optionally-substituted  $C_{6-10}$  aryl;

$R_4$  and  $R_5$  together with the nitrogen to which they are attached form a ring having 4 or 5 carbon atoms, which ring optionally contains 1 or 2 additional heteroatoms independently selected from the group consisting of the group consisting of -O-, -S- and -NR<sub>6</sub>-, wherein  $R_6$  is hydrogen,  $C_{1-6}$  alkyl,  $C_{1-6}$  haloalkyl or  $C_{1-6}$  hydroxyalkyl; and

X is -O-, -S-, -CH<sub>2</sub>-O- or -CH<sub>2</sub>-S-.

49. The method according to claim 41, wherein  $R_3$  is  $\begin{array}{c} R_7 \\ || \\ -C-R_8 \end{array}$ ,  
wherein:

$R_7$  is oxygen;

$R_8$  is  $C_{1-6}$  alkyl,  $C_{1-6}$  haloalkyl,  $C_{1-6}$  hydroxyalkyl, optionally-substituted  $C_{5-6}$  cycloalkyl or optionally-substituted phenyl;

$R_4$  and  $R_5$  together with the nitrogen to which they are attached form a ring having 4 or 5 carbon atoms, which ring optionally contains 1 or 2 additional heteroatoms selected from the group consisting of -O-, -S-, and -NR<sub>6</sub>-, wherein  $R_6$  is hydrogen or  $C_{1-6}$  alkyl;

$n$  is 1 or 2;

$R_1$  is halogen,  $C_{1-6}$  alkyl or  $C_{1-6}$  haloalkyl;

X is -O- or -S-; and

$m$  is 2 or 3.

50. The method according to claim 41, wherein  $R_3$  is  $\begin{array}{c} R_7 \\ || \\ -C-R_8 \end{array}$ ,  
wherein:

$R_7$  is oxygen;

$R_8$  is  $C_{1-6}$  alkyl,  $C_{5-6}$  cycloalkyl or phenyl, wherein the phenyl is substituted with zero, 1 or 2, groups independently selected from the group consisting of halogen,  $C_{1-6}$  alkyl,  $C_{1-6}$  haloalkyl,  $C_{1-6}$  hydroxyalkyl,  $C_{1-6}$  alkyloxy( $C_{1-6}$ )alkyl, amino( $C_{1-6}$ )alkyl, hydroxy, nitro and amino;

$R_4$  and  $R_5$  together with the nitrogen to which they are attached form a ring having 4 or 5 carbon atoms, which ring optionally contains 1 additional heteroatom independently selected from the group consisting of -O-, -S- and -NR<sub>6</sub>-, wherein  $R_6$  is hydrogen,  $C_{1-6}$  alkyl,  $C_{1-6}$  haloalkyl or  $C_{1-6}$  hydroxyalkyl;

$n$  is 1;

$R_1$  is  $C_{1-6}$  haloalkyl;

$X$  is -O-; and

$m$  is 2.

51. The method according to claim 41, wherein  $R_3$  is  $\begin{array}{c} R_7 \\ || \\ -C-R_8 \end{array}$ ,  
wherein:

$R_7$  is oxygen or sulfur;

$R_8$  is optionally-substituted  $C_{1-6}$  alkyl, optionally-substituted  $C_{3-8}$  cycloalkyl or optionally-substituted  $C_{6-10}$  aryl;

$R_4$  and  $R_5$  are independently selected from the group consisting of hydrogen and optionally-substituted  $C_{1-6}$  alkyl; and

$X$  is -O-, -S-, -CH<sub>2</sub>-O- or -CH<sub>2</sub>-S-.

52. The method according to claim 41, wherein  $R_3$  is  $\begin{array}{c} R_7 \\ || \\ -C-R_8 \end{array}$ ,  
wherein:

R<sub>7</sub> is oxygen;

R<sub>8</sub> is C<sub>1-6</sub> alkyl, C<sub>1-6</sub> haloalkyl, C<sub>1-6</sub> hydroxyalkyl, optionally-substituted C<sub>5-6</sub> cycloalkyl or optionally-substituted phenyl;

R<sub>4</sub> and R<sub>5</sub> are independently selected from the group consisting of hydrogen, C<sub>1-6</sub> alkyl and C<sub>1-6</sub> haloalkyl;

*n* is 1 or 2;

R<sub>1</sub> is halogen, C<sub>1-6</sub> alkyl or C<sub>1-6</sub> haloalkyl;

X is -O- or -S-; and

*m* is 2 or 3.

53. The method according to claim 41, wherein R<sub>3</sub> is  $\begin{array}{c} \text{R}_7 \\ || \\ \text{---C---R}_8 \end{array}$ , wherein:

R<sub>7</sub> is oxygen;

R<sub>8</sub> is C<sub>1-6</sub> alkyl, C<sub>5-6</sub> cycloalkyl or phenyl, wherein the phenyl is substituted with zero, 1 or 2 groups independently selected from the group consisting of halogen, C<sub>1-6</sub> alkyl, C<sub>1-6</sub> haloalkyl, C<sub>1-6</sub> hydroxyalkyl, C<sub>1-6</sub> alkyloxy(C<sub>1-6</sub>)alkyl, amino(C<sub>1-6</sub>)alkyl, hydroxy, nitro and amino;

R<sub>4</sub> and R<sub>5</sub> are independently selected from the group consisting of hydrogen and C<sub>1-6</sub> alkyl;

*n* is 1;

R<sub>1</sub> is C<sub>1-6</sub> haloalkyl;

X is -O-; and

*m* is 2.

54. The method according to claim 41, wherein R<sub>3</sub> is

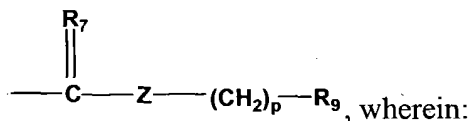
$\begin{array}{c} \text{R}_7 \\ || \\ \text{---C---Z---(CH}_2\text{)}_p\text{---R}_9 \end{array}$ , wherein:

R<sub>9</sub> is optionally-substituted C<sub>1-6</sub> alkyl, optionally-substituted C<sub>3-8</sub> cycloalkyl, optionally-substituted C<sub>6-10</sub> aryl, optionally-substituted heteroaryl or optionally-substituted saturated or partially unsaturated heterocycle;

R<sub>4</sub> and R<sub>5</sub> together with the nitrogen to which they are attached form a ring having 4 or 5 carbon atoms, which ring optionally contains 1 or 2 additional heteroatoms independently selected from the group consisting of -O-, -S- and -NR<sub>6</sub>-, wherein R<sub>6</sub> is hydrogen, C<sub>1-6</sub> alkyl, C<sub>1-6</sub> haloalkyl or C<sub>1-6</sub> hydroxyalkyl; and

X is -O-, -S-, -CH<sub>2</sub>-O- or -CH<sub>2</sub>-S-.

55. The method according to claim 41, wherein R<sub>3</sub> is



R<sub>7</sub> is oxygen;

Z is -NH-;

p is zero, 1, 2 or 3;

R<sub>9</sub> is C<sub>1-6</sub> alkyl, C<sub>1-6</sub> haloalkyl, C<sub>1-6</sub> hydroxyalkyl, optionally-substituted C<sub>5-6</sub> cycloalkyl, optionally-substituted phenyl or optionally-substituted 5- to 6-membered saturated or partially unsaturated heterocycle;

R<sub>4</sub> and R<sub>5</sub> together with the nitrogen to which they are attached form a ring having 4 or 5 carbon atoms, which ring optionally contains 1 or 2 additional heteroatoms selected from the group consisting of -O-, -S-, and -NR<sub>6</sub>-, wherein R<sub>6</sub> is hydrogen or C<sub>1-6</sub> alkyl;

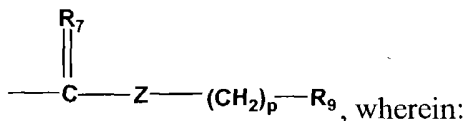
n is 1 or 2;

R<sub>1</sub> is halogen, C<sub>1-6</sub> alkyl or C<sub>1-6</sub> haloalkyl;

X is -O- or -S-; and

m is 2 or 3.

56. The method according to claim 41, wherein  $R_3$  is



$R_7$  is oxygen;

$Z$  is -NH-;

$p$  is zero, 1, 2 or 3;

$R_9$  is  $C_{5-6}$  cycloalkyl, optionally-substituted phenyl or 5- to 6-membered saturated or partially unsaturated heterocycle, wherein the phenyl is substituted with zero, 1 or 2 groups independently selected from the group consisting of halogen,  $C_{1-6}$  alkyl,  $C_{1-6}$  haloalkyl,  $C_{1-6}$  hydroxyalkyl,  $C_{1-6}$  alkyloxy( $C_{1-6}$ )alkyl, amino( $C_{1-6}$ )alkyl, hydroxy, nitro and amino;

$R_4$  and  $R_5$  together with the nitrogen to which they are attached form a ring having 4 or 5 carbon atoms, which ring optionally contains 1 additional heteroatom independently selected from the group consisting of -O-, -S- and -NR<sub>6</sub>-, wherein  $R_6$  is hydrogen,  $C_{1-6}$  alkyl,  $C_{1-6}$  haloalkyl or  $C_{1-6}$  hydroxyalkyl;

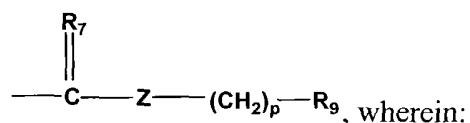
$n$  is 1;

$R_1$  is  $C_{1-6}$  haloalkyl;

$X$  is -O-; and

$m$  is 2.

57. The method according to claim 41, wherein  $R_3$  is

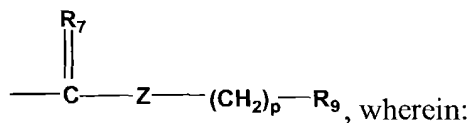


$R_9$  is optionally-substituted  $C_{1-6}$  alkyl, optionally-substituted  $C_{3-8}$  cycloalkyl, optionally-substituted  $C_{6-10}$  aryl, optionally-substituted heteroaryl or optionally-substituted saturated or partially unsaturated heterocycle;

$R_4$  and  $R_5$  are independently selected from the group consisting of hydrogen and optionally-substituted  $C_{1-6}$  alkyl; and

$X$  is -O-, -S-, -CH<sub>2</sub>-O- or -CH<sub>2</sub>-S-.

58. The method according to claim 41, wherein  $R_3$  is



$R_7$  is oxygen;

$Z$  is -NH-;

$p$  is zero, 1, 2 or 3;

$R_9$  is  $C_{1-6}$  alkyl,  $C_{1-6}$  haloalkyl,  $C_{1-6}$  hydroxyalkyl, optionally-substituted  $C_{5-6}$  cycloalkyl, optionally-substituted phenyl or optionally-substituted 5- to 6-membered saturated or partially unsaturated heterocycle;

$R_4$  and  $R_5$  are independently selected from the group consisting of hydrogen,  $C_{1-6}$  alkyl and  $C_{1-6}$  haloalkyl;

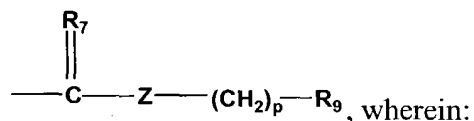
$n$  is 1 or 2;

$R_1$  is halogen,  $C_{1-6}$  alkyl or  $C_{1-6}$  haloalkyl;

$X$  is -O- or -S-; and

$m$  is 2 or 3.

59. The method according to claim 41, wherein  $R_3$  is



$R_7$  is oxygen;

$Z$  is -NH-;

$p$  is zero, 1, 2 or 3;

$R_9$  is  $C_{5-6}$  cycloalkyl, optionally-substituted phenyl or 5- to 6-membered saturated or partially unsaturated heterocycle, wherein the phenyl is substituted with zero, 1 or 2, preferably zero or one, groups independently selected from the group consisting of halogen,  $C_{1-6}$  alkyl,  $C_{1-6}$  haloalkyl,  $C_{1-6}$  hydroxyalkyl,  $C_{1-6}$  alkyloxy( $C_{1-6}$ )alkyl, amino( $C_{1-6}$ )alkyl, hydroxy, nitro and amino;

$R_4$  and  $R_5$  are independently selected from the group consisting of hydrogen and  $C_{1-6}$  alkyl;

$n$  is 1;

$R_1$  is  $C_{1-6}$  haloalkyl;

$X$  is -O-; and

$m$  is 2.

60. The method according to claim 41, wherein said disorder is selected from the group consisting of neuronal damage, acute or chronic pain, neuropathic pain, surgical pain, convulsions, a neurodegenerative condition, manic depression and diabetic neuropathy.

61. The method according to claim 41, wherein said disorder is acute or chronic pain.

62. The method according to claim 41, wherein said disorder is neuropathic pain.

63. The method according to claim 41, wherein said disorder is surgical pain.

64. The method according to claim 41, wherein said disorder is neuronal damage caused by focal or global ischemia.

65. The method according to claim 41, wherein said disorder is a neurodegenerative condition.

66. The method according to claim 65, wherein said neurodegenerative condition is amyotrophic lateral sclerosis (ALS).

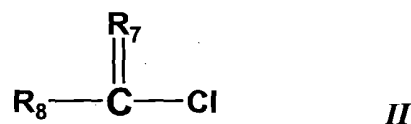
67. The method according to claim 41, wherein said compound functions as an antitinnitus agent, an anticonvulsant, an antiarrhythmic, a local anesthetic or an antimaniac depressant.

68. The method according to claim 41, wherein said mammal is a human, dog or cat.

69. The method according to claim 41, wherein said mammal is a human.

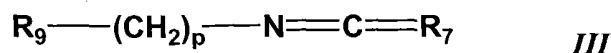
70. A method of making the compound according to claim 1, wherein said method comprises:

- (a) reacting in a first step an aryl aldehyde with a primary or secondary amine;
- (b) optionally, in a second step, reacting the product of the first step (i) with an acid chloride compound of Formula *II*:



wherein R<sub>7</sub> is oxygen or sulfur, and R<sub>9</sub> is selected from the group consisting of optionally-substituted C<sub>1-6</sub> alkyl, an optionally-substituted C<sub>3-8</sub> carbocyclic ring system, or an optionally-substituted C<sub>6-10</sub> aryl;

(ii) with an isocyanate of Formula *III*:



wherein *p* is an integer from zero to 4, R<sub>7</sub> is oxygen or sulfur, and R<sub>9</sub> is selected from the group consisting of optionally-substituted C<sub>1-6</sub> alkyl, an optionally-substituted C<sub>3-8</sub> carbocyclic ring system, optionally-substituted C<sub>6-10</sub> aryl, optionally-substituted heteroaryl and saturated or partially unsaturated heterocycle;



or (iii) with either triphosgene and triethylamine or thiophosgene and triethylamine, followed by

$R_9-(CH_2)_p-OH$ , wherein  $p$  is an integer from zero to 4, and  $R_9$  is selected from the group consisting of optionally-substituted  $C_{1-6}$  alkyl, an optionally-substituted  $C_{3-8}$  carbocyclic ring system, optionally-substituted  $C_{6-10}$  aryl, optionally-substituted heteroaryl and saturated or partially unsaturated heterocycle; and

- (c) recovering the product obtained from either of the first or second steps.